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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BLUMEL, BENJAMIN P

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/575,279	Applicant(s) OOMENS ET AL.	
	Examiner BENJAMIN P. BLUMEL	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 5, 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 56-106 is/are pending in the application.
- 4a) Of the above claim(s) 57,59,60,62-64,66-69,71-75,77-81 and 84-105 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 56,58,61,65,70,76,82,83 and 106 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/07/06</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of invention I in the reply filed on May 5, 2008 is acknowledged.

Claims 57, 59, 60, 62-64, 66-69, 71-75, 77-81, 84-105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 5, 2008.

Claims 56, 58, 61, 65, 70, 76, 82, 83 and 106 are examined on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on November 7, 2006 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65, 82 and 83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a recombinant RSV (rRSV) having baculovirus GP64 with the recited limitations regarding infectivity stability, does not reasonably provide enablement for making any enveloped recombinant vertebrate virus with those same infectivity stability properties. The specification does not enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The claims encompass any enveloped recombinant vertebrate virus comprising a heterologous envelope protein, wherein said envelope protein is capable of mediating entry of the recombinant virus into a mammalian cell, wherein the recombinant virus has been stored at above 0°C for at least 3.5 days, wherein infectivity of the recombinant virus at the end of said at least 3.5 days is at least 60% of that at the beginning of said at least 3.5 days, and wherein said storage conditions are such that the average infectivity of a wild-type virus of the same species as the recombinant virus is reduced by more than 40% after said at least 3.5 days under said storage conditions. The nature of the invention is the construction of recombinant viruses that can be stored at a temperature above 0°C for at least 3.5 days without significant loss of infectivity. Applicant's discovery regarding the storage conditions and infectivity stability appears to relate to the substitution of the native envelope protein for a heterologous envelope protein. Applicant has not demonstrated that the substitution of any viral envelope protein will result in a virus having the claimed infectivity stability. Applicant discloses that the substitution of a baculovirus envelope protein GP64 for the host viral envelope imparts enhanced stability of infectivity to recombinant viruses (see paragraph [0066]). Applicant's only other specific guidance for

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choosing other envelope proteins is orthomyxoviruses, including Thogoto or Dhori viruses.

Without further guidance relating to appropriate envelope proteins that can be substituted for host viral envelope proteins that result in the claimed infectivity stability, one of skill in the art would not know how to make other recombinant viruses with those same properties. The working examples only relate to recombinant Human RSV in combination with GP64, and the specification's only additional guidance for choosing envelope proteins is that other vertebrate viruses can be employed. Therefore, since numerous enveloped vertebrate viruses exist, but applicants have only considered one (HRSV) in combination with GP64, additional research would need to be conducted to determine if other enveloped vertebrate viruses in combination with GP64, or other non-GP64 substitute envelope proteins in combination with enveloped vertebrate viruses, such as vaccinia or herpes simplex virus, would have the stability as instantly claimed under the same storage conditions.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 65, 82 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 65 and 82 recite, "...has been stored under storage conditions...", however, it is unclear what the meets and bounds of the term "storage conditions" are. Claim 83 is rejected since it depends from claim 82.

Claim 83 recites, "...maintaining storage temperature or temperatures at above...".

However, it is unclear why would more than one temperature be maintained. Is this implying

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that multiple temperatures are tested for their effects on reducing viral infectivity as recited in claim 82?

Claim Objections

Claim 106 is objected to because of the following informalities: Since the acronym for the RSV SH protein is not as well known as the acronym "DNA", it is suggested that the claim also recite "small hydrophobic". Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 56, 58, 70, 76 and 106 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7,041,489 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented invention is drawn to a recombinant RSV in which the G, F and SH proteins are deleted and replaced by a gene encoding a heterologous chimeric protein of a

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cytoplasmic domain of RSV F protein and either the G protein of Vesicular Stomatitis Virus (VSV) or the GP64 protein from baculovirus. Therefore, the instant invention is anticipated since it is also drawn to a either: A recombinant respiratory syncytial virus (RSV) comprising a nonparamyxoviral envelope protein capable of mediating entry of said recombinant RSV into a mammalian cell, wherein said envelope protein comprises an ectodomain of a baculovirus envelope GP64 protein, and wherein said recombinant RSV lacks endogenous RSV SH protein; or a recombinant virus from the *Paramyxoviridae* family in which a heterologous envelope protein of the ectodomain and transmembrane domain of baculovirus GP64 and the C-terminus of a RSV F protein are expressed by the rRSV (a immunogenic epitope of a mammalian pathogen).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 56, 58, 61, 70 and 76 are rejected under 35 U.S.C. 102(a) as being anticipated by Wertz et al. (WO 03/029416 A).

The claimed invention is drawn to a recombinant virus from the *Paramyxoviridae* family in which a heterologous envelope protein of the ectodomain and transmembrane domain of baculovirus GP64 and the C-terminus of a RSV F protein are expressed by the rRSV (a immunogenic epitope of a mammalian pathogen).

Wertz et al. teach a recombinant virus of the *Paramyxoviridae* family comprising a

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nonparamyxoviral envelope protein capable of mediating entry of said recombinant virus into a mammalian cell, e.g. hRSV particles carrying baculoviral gp64, or a fusion protein consisting of the baculoviral gp64 and amino acids 563-574 of hRSV's F protein (p.49 In.4-7); heterologous envelope protein ORF provided in cis or in trans (with corresponding effect on transmissibility); inclusion of marker genes; pH dependency, fusion competency, temperature sensitivity, control over transmission and target tissue, high titers and stability are all properties described for said recombinant viruses. *See example 12 and pages 49 and 51-54..* Therefore, Wertz et al. anticipate the claimed invention.

Claim 106 is rejected under 35 U.S.C. 102(a) as being anticipated by Wertz et al. (*supra*).

A recombinant respiratory syncytial virus (RSV) comprising a nonparamyxoviral envelope protein capable of mediating entry of said recombinant RSV into a mammalian cell; wherein said envelope protein comprises an ectodomain of a baculovirus envelope GP64 protein; and wherein said recombinant RSV lacks endogenous RSV SH protein.

Wertz et al. teach the generation of a recombinant RSV which lacks the small hydrophobic (SH) protein and can express either the ectodomain of baculovirus GP64 or VSV G proteins. These heterologous proteins function as entry proteins for mammalian target cells. Therefore, Wertz et al. anticipate the claimed invention. *See pages 51-54.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 56 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wertz et al. (WO 03/029416 A) and Parrington et al. (WO 02/09749 A2).

The claimed invention is also drawn to the rRSV that has also been incorporated into a pharmaceutical composition which has been stored at above about 0°C for at least 3.5 days.

The teachings of Wertz et al. are discussed above, however they do not teach storing such a composition at above about 0°C for at least 3.5 days.

Parrington et al. teach the storage of RSV compositions at various temperatures in order to test the stability of the virus. Some examples of such temperatures are 5°C for 42 months, 25°C for 5 months and 37°C for 5 weeks. *See paragraph 65.*

It would have been obvious to one of ordinary skill in the art to modify the compositions taught by Wertz et al. in order to store the rRSV at above about 0°C for at least 3.5 days. One would have been motivated to do so, given the suggestion by Wertz et al. that the compositions should be kept stable. There would have been a reasonable expectation of success, given the knowledge that similar storage conditions were previously used with RSV, as taught by Parrington et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Summary

No claims are allowed.

Conclusion

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stacy B Chen/
Primary Examiner, Art Unit 1648

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648